

STATUS OF THE CLAIMS

Claims 1-19 and 21-29 and 31 are pending herein, claim 20 having been canceled herein. Claims 1 and 21 are the independent claims. Claims 24-29 were previously withdrawn pursuant to a restriction requirement and claim 30 has been previously canceled. Thus, claims 1-19, 21-23 and 31 are presented for examination.

Further to the Examiner's comments in the Advisory Action, the claims have been amended specifically recite that the second fluid is injected subsequent to the first fluid.

Rejection under 35 U.S.C. §112

Claim 20 was rejected in the Final Office Action under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. Specifically, the Office Action notes that it is unclear if the therapeutic agent of claim 20 is the same as that recited in claim 1, or if claim 20 is referring to a second therapeutic agent.

Although not mentioned in the Advisory Action, this rejection is believed to be moot in view of the prior cancelation of claim 20.

Rejection under 35 U.S.C. §103(a) – Sawhney in view of Weikel et al.

Claims 1-9, 11-23 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawhney (US 6,818,018 "Sawhney") in view of Weikel et al. (U.S. Patent No. 6,632,235 "Weikel"). Applicant respectfully traverses this rejection.

For a proper obviousness rejection under 35 U.S.C. 103, the differences between the subject matter sought to be patented and the prior art must be such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. 35 U.S.C. §103. The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. MPEP 2141. " '[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.' " *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385 (2007), quoting *In re Kahn*, 441 F.3d 977, 988, (Fed. Cir.

2006). It should be noted that the prior art reference (or references when combined) must teach or suggest all the claimed features. “When determining whether a claim is obvious, an examiner must make ‘a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art.’ ... Thus, ‘obviousness requires a suggestion of all limitations in a claim.’ ...” *Ex parte Wada and Murphy*, BPAI Appeal No. 2007-3733, January 14, 2008 (emphasis in original) (citations omitted). In addition, there must be a reasonable expectation of success. See MPEP 2143.02.

All presently pending claims require a method that comprises the following: (a) injecting a first fluid comprising a non-crosslinkable polymer into a container that is positioned within the subject, (b) injecting a second fluid comprising a crosslinkable polymer into said container, said second fluid having a lower viscosity than said first fluid and wherein said second fluid coats the first fluid; (c) crosslinking said crosslinkable second polymer in said container by introducing a crosslinking agent to said container, thereby forming a crosslinked polymeric body comprising a first fluid coated with a solid or semisolid crosslinked polymer in said container; and (d) releasing said crosslinked solid polymeric body into said subject.

Such a method is unobvious over Sawhney and Weikel.

For example, Sawhney is directed to compositions and methods for forming hydrogels *in situ* through a combination of physical and chemical crosslinking processes wherein physical crosslinking is mediated by one or more natural or synthetic components that stabilize a hydrogel-forming precursor solution at a deposition site for a period of time sufficient for more resilient chemical crosslinks to form (Abstract). In this regard, physical crosslinking is typically a more rapid process than chemical crosslinking; however, it does not lead to the formation of mechanically resilient or stable hydrogels (col. 5, lines 49-58). Consequently, physical crosslinking of the hydrogel precursor solutions is able to proceed rapidly upon introduction of the precursor solutions at the deposition site, serving to localize or confine the hydrogel forming precursors at that site (col. 6, lines 17-21).

Delivery systems suitable for delivering the hydrogel systems described in Sawhney involve the introduction of a water soluble crosslinking agent (WSCA) solution and a water soluble crosslinkable polymer (WSCP) solution. Col. 18, lines 50-58.

At page 3 of the Office Action, it is stated that Sawhney discloses the invention substantially as claimed including injecting a crosslinkable polymer (second fluid) and crosslinking agent to a target location within the body, such that the crosslinkable polymer is crosslinked in situ to form a solid or semisolid crosslinked polymer at the target location.

The Examiner further argues that (emphasis added) “*a first fluid comprising a non-crosslinkable polymer* (release rate modification agent - col 18, ll 23-38) and a therapeutic agent (col 16, ln 10 – col 17, ln 65) is injected along with the *crosslinkable polymer* and *crosslinking agent*, such that the crosslinkable polymer coats the first fluid to form a solid crosslinked polymer containing the first fluid upon reaction of the crosslinkable polymer with the crosslinking agent (col 15, ln 66 – col 16, ln 2).

However, while Sawhney may remotely resemble the present invention in describing a method involving (a) “injecting a second fluid comprising a crosslinkable polymer” (i.e., a WSCP solution) and (b) “crosslinking said crosslinkable second polymer of said second fluid ... by introducing a crosslinking agent” (i.e., a WSCA solution), Sawhney is deficient in several ways not recognized by the Office Action.

First, Sawhney does not teach (a) *injecting a first fluid comprising a non-crosslinkable polymer* in addition to (b) injecting a second fluid comprising a crosslinkable polymer and (c) crosslinking the crosslinkable second polymer in the container by introducing a crosslinking agent.

In this regard, Sawhney merely teaches injecting a crosslinkable polymer solution (i.e., a WSCP solution) and a crosslinking agent solution (i.e., a WSCA solution). The release rate modification agent (which the Office Action is construing as the presently claimed non-crosslinkable polymer) is not taught to be applied independently of the crosslinkable polymer and crosslinking agent solutions. The section on “Delivery of Bioactive Species” spanning cols. 15-18 of Sawhney lists several release rate modification agents and notes that these agents can be used singly or in combination with other such agents (col. 18, lines 40-47). This section also notes that the release rate modifying agents “may be used in conjunction with hydrogels of the current invention” (col. 17, line 66 to col. 18 line 2) and that preferably “the release rate modification agent is compatible with the combination of polymers and solvent used to

formulate the polymer solution” (col. 18, lines 19-22). Each of the preceding statements indicates that the release rate modification agent is to be applied *with* the hydrogel forming polymer in the crosslinkable polymer solution, rather than independently of such a solution.

In the Advisory Action it is argued that the claims do not require the first fluid to be injected independently of the first fluid and that simultaneous injection of the first and second fluids meets the claimed inventions. In view of the above amendment, the claims clearly no longer read on simultaneous injection of the first and second fluids.

The Office Action states that Sawhney disclose several polymer choices for both *the non-crosslinkable polymer of the first fluid* and the crosslinkable polymer of the second fluid. However the citations given in the Office Action (which are from the section on Delivery of Bioactive Species spanning cols. 15-18 of Sawhney) do not support this assertion.

Sawhney does not describe a process in which a first fluid comprising a non-crosslinkable polymer (i.e., a first solution comprising a release rate modification agent) is combined with a second fluid comprising a crosslinkable polymer at all, much less one where the second fluid has a lower viscosity than the first fluid and wherein the second fluid coats the first fluid as claimed.

On page 3 of the Office Action, the Examiner makes the following argument regarding obviousness:

It would have been prima facie obvious to try modifying the method of Sawhney to choose the materials such that the chosen crosslinkable polymer for the second material was less viscous than the chosen non-crosslinkable polymer for the first material to allow the second material to sufficiently coat the second material in an attempt to provide an improved drug loaded hydrogel as a person with ordinary skill has good reason to pursue the known options within his or her technical grasp and since it is obvious to choose from a finite number of identified, predictable solutions with a reasonable expectation of success.

This assertion, however, is flawed. For example, as noted above, Sawhney does *not* describe a process in which a first fluid comprising a non-crosslinkable polymer is applied independently of a second fluid comprising a crosslinkable polymer.

Moreover, even assuming *solely* for the sake of argument Sawhney did teach the use of a first fluid comprising a non-crosslinkable polymer and a second fluid comprising a crosslinkable

polymer, the concept of the “second fluid having a lower viscosity than said first fluid and wherein said second fluid coats said first fluid” is *Applicant’s concept* and is not at all obvious over Sawhney. See MPEP 2142: “... impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.”

The Office Action agrees that Sawhney does not teach injection of hydrogel forming compositions described therein into a container positioned within the target location. To make up for this deficiency in Sawhney, the Office Action turns to Wiekel arguing the following: (a) Wiekel discloses a similar method for forming a crosslinking a polymer in situ and teach the crosslinking agent and crosslinkable polymer are injected into a container positioned within the subject; (b) by injecting the elements into a container placed within the subject, more controlled deployment of the crosslinked polymer may be obtained and the risk of polymeric precursors to other areas of the body is reduced; (c) upon solidification of the polymer, the container may be removed to release the solidified polymer within the target area.

Based on the preceding, the Office Action concludes that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Sawhney such that first fluid, second fluid, and crosslinking agent were injected into a container placed within the target location as taught by Wiekel to ensure the first fluid, second fluid, and crosslinking agent do not migrate from the target location prior to solidification/crosslinking of the second fluid.” Applicant respectfully disagrees.

First Sawhney is deficient for several reasons, including the fact that it does not teach or suggest a distinct first fluid, second fluid, and crosslinking agent as urged in the Office Action. While it is true that Sawhney teaches a crosslinkable polymer solution (i.e., a WSCP solution) and a crosslinking agent solution (i.e., a WSCA solution), Sawhney does not teach “a first fluid comprising a non-crosslinkable polymer” as claimed at all, much less a system comprising a “second fluid [comprising a crosslinkable polymer] having a lower viscosity than said first fluid and wherein said second fluid coats said first fluid”.

Second, there would be no reason to modify Sawhney to use a container as taught by Weikel to ensure that the fluids taught by Sawhney (i.e., the crosslinkable polymer solution and the crosslinking agent solution) do not migrate from the target location, because Sawhney has

solved this problem in another way. Specifically, as noted above, Sawhney describes a system whereby physical crosslinking of the hydrogel precursor solutions proceeds rapidly upon introduction of the precursor solutions at the deposition site, and serves to localize or confine the hydrogel forming precursors at that site for a period of time sufficient for more resilient chemical crosslinks to form (Abstract and col. 6, lines 17-21).

Stated another way, if a container as described in Weikel were employed, the compositions of Sawhney would no longer operate to stabilize hydrogel-forming precursor solutions at a deposition site for a period of time sufficient for more resilient chemical crosslinks to form (see Abstract). “If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.” MPEP 2143.01 VI (citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)).

For at least the foregoing reasons, claims 1-9, 11-23 and 31 patentable under 35 U.S.C. 103(a) over Sawhney and Weikel.

Rejection under 35 U.S.C. §103(a) – Sawhney and Weikel et al. in view of Spacek

Claim 10 is rejected under 35 U.S.C. §103(a) as obvious over Sawhney and Weikel in view of Spacek (U.S. Patent No. 6,524,327 “Spacek”). Applicant respectfully traverses this rejection.

For example, claim 1 from which claim 10 depends is patentable over Sawhney and Weikel for the reasons set forth above. Spacek, which is cited for its alleged teachings regarding washing a crosslinked polymeric body prior to releasing the crosslinked solid polymeric body, does not make up for the above-noted deficiencies in Sawhney and Weikel.

For at least the foregoing reasons, claim 10 is patentable under 35 U.S.C. 103(a) over Sawhney, Weikel and Spacek.

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CONCLUSION

In view of the above, Applicant submits that all pending claims are in condition for allowance. If the Examiner believes there are still unresolved issues, a telephone call to the undersigned would be welcomed.

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